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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,122	09/24/2003	Salim Yusuf	16554-002001	2547

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EXAMINER	
VENCI, DAVID J	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/670,122	YUSUF ET AL.	
	Examiner	Art Unit	
	David J Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/15/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

The specification is objected to because the specification appears to interchangeably recite both "pg/mmol" and "ng/mmol" units of measurement. Clarification is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, for being incomplete or omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claims 1 and 3 do not accomplish the stated purpose of "assessing aspirin resistance" because both claims do not set forth a step for assessing aspirin resistance.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, because "the second, third or fourth quartile" lacks antecedent basis.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, because "the immunoassay" lacks antecedent basis.

Claims 10-15 are rejected under 35 U.S.C. 112, second paragraph, because the name "11-dihydro thromboxane" refers to an unknown compound. Applicants may wish to amend the claims to recite "11-dehydro thromboxane."

Claims 4, 10-13 and 16-17 are rejected under 35 U.S.C. 112, second paragraph, for the recitation of "risk." The type of "risk" is not clear because "risk" and "relative risk" appear to be used interchangeably in the claims. Clarification is required. In addition, the context of the "risk" (i.e. a defined set of circumstances) is not clear. The recitation of "in a patient taking aspirin" or "an increased concentration of the thromboxane A2 metabolite" does not sufficiently define the context or circumstances involving "risk" absent a baseline for comparision. Applicants may wish to amend claims 4 and 17 to include a limitation reciting a baseline concentration value of thromboxane A2 metabolite.

Claims 10-15 rejected under 35 U.S.C. 112, second paragraph, for the recitation of "pg/mmol" unit of measurement. The "pg/mmol" and "ng/mmol" units of measurement appear to be used interchangeably throughout the claims. Clarification is required.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, for the recitation of "less than between." The numeric range of "less than between" is not clear.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, for the recitation of "providing a readout." The term "readout" is vague and indefinite, and it appears that the term "readout" is not defined in the specification.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, because "the standardized quartile concentrations," "the first quartile," "the second quartile," "the third quartile," and "the fourth quarter" lack antecedent basis. Also, the recitation of a "fourth quarter" is vague.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-13 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, it is unclear how the various risk percentages are derived. The claimed 15% in claim 12 appears to have no support in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-9 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Ens (WO 01/31052).

With respect to claim 1, Ens describes a method for assessing aspirin resistance (See Example 2, p. 10, line 23) in a patient by measuring a thromboxane A2 metabolite (See Example 2, p. 10, line 19, "11-dehydro TXB_2") in a sample of body fluid (See Example 2, p. 10, line 19, "Urine").

With respect to claim 4, Ens describes a method for assessing risk of a cardiovascular event (See Example 2, p. 11, line 19, "potential thrombotic events") in a patient taking aspirin (See Example 2, p. 11, line 17, "aspirin users") by measuring a thromboxane A2 metabolite (See Example 2, p. 10, line 19, "11-dehydro TXB_2") in a sample of biological fluid (See Example 2, p. 10, line 19, "Urine"), wherein an increased concentration of metabolite (See Example 2, p. 11, lines 17-18, "six individuals (13%) had results above the decision point and two exceeded the aspirin effect rule-out point of 1000") correlates with an increased risk of a cardiovascular event (See Example 2, p. 11, line 19, "potential thrombotic events").

With respect to claim 5, Ens describes a method wherein a patient has arterial vascular disease (See Summary of the Invention, p. 7, lines 24-26, "The present invention... provides a method for identifying... aspirin dose for a patient...") (See also Background of the Invention, p. 3, lines 10-12, "Aspirin is indicated for patients with stable angina, unstable angina, acute myocardial infarction, transient cerebral ischemia, thrombotic stroke, and peripheral arterial disease") (emphasis added).

With respect to claims 6-7, Ens describes a method wherein ELISA (See Example 2, p. 10, line 29, "acetylcholinesterase-linked enzyme immunoassay") is used to determine the concentration of thromboxane-A2 metabolite.

With respect to claim 8, Ens describes a method using urine (See Example 2, p. 10, line 19, "Urine").

With respect to claim 9, Ens describes a method wherein 11-dehydro-TXB_2 is measured (See Example 2, p. 10, line 19, "11-dehydro TXB_2").

With respect to claim 17, Ens describes a method of screening for risk of a cardiovascular event (See Example 2, p. 11, line 19, "potential thrombotic events"). The enzyme immunoassay of Ens (See Example 2, p. 10, line 29, "acetylcholinesterase-linked enzyme immunoassay") necessarily contains the steps of "contacting a body fluid sample from the patient with an antibody which specifically binds to a thromboxane-A2 metabolite" and "determining the degree of immune complex formation", and would be so recognized by persons of skill in the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

> skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3 and 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ens (WO 01/31052) in view of Cipollone et al., 102 CIRCULATION 1007 (2000) and Encyclopedia of Biostatistics, Armitage & Colton, Eds. (1998) (hereinafter "Armitage & Colton").

Ens describes a method for assessing aspirin resistance and a method for assessing risk of cardiovascular event, as substantially described *supra*. In addition, Ens suggests the performance of clinical trials to compare biologic response to aspirin's affect on clinical outcomes (See Example 3, p. 13, line 7-9).

Ens does not teach the step of creating a predetermined set of concentration quartiles for comparing 11-dehydro-TXB_2 concentrations in a patient sample. Ens does not teach particular risks associated with particular thromboxane concentrations associated with said quartiles.

However, Armitage & Colton teach the use of quantiles, including division into quartiles, as a useful tool for modeling risk relationships (See pp 3628-9). In addition, Armitage & Colton teach the use of nested case-contol studies to determine risks through the estimation of odds ratios from logistic regression (See p. 17, col. 1, Estimation from Population-Based or Nested Case-Control Studies, first paragraph). Cipollone et al. teach a similar range (17.0–28.3 ng/mmol) of 11-dehydro-TXB_2 concentrations in patients taking aspirin (See p. 1010, Fig. 6(right), estimating 11-dehydro-TXB_2 concentration range is approximately 150 - 250 pg/mg in patients taking aspirin, and assuming creatinine MW = 113.12 g/mol).

Therefore, it would have been obvious for a person of ordinary skill in the art to combine the method for assessing aspirin resistance and risk of cardiovascular event, as taught by Ens, with the method of using quantiles and the method of determining risks through the estimation of odds ratios from logistic regression in a nested case-control study, as taught by Armitage & Colton, and the 11-dehydro-TXB_2 concentration range, as taught by Cipollone et al., in order to provide a method for assessing risk of a cardiovascular event by comparing 11-dehydro-TXB_2 concentrations in a patient sample against a predetermined set of concentration quartiles.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci
Examiner
Art Unit 1641

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07/12/04